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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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*Ex parte* KISHORE K. WARY and JOSEPH O. HUMTSOE

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Appeal 2009-006644
Application 10/812,238
Technology Center 1600

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Decided: March 12, 2010

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Before TONI R. SCHEINER, DEMETRA J. MILLS, and
ERIC GRIMES, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for anticipation and obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

## STATEMENT OF CASE

The following claims are representative.

8. A method of inhibiting αvβ3 and/or α5β1 integrin ligand-mediated cell-cell interaction, comprising:

contacting the cells with an antibody directed against a peptide consisting of SEQ ID NO: 41 or consisting of SEQ ID No. 2 that is derived from a cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP) consisting of SEQ ID No. 13, wherein said contact with the antibody blocks binding of αvβ3 and/or α5β1 integrins to the cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP), thereby inhibiting the αvβ3 and/or α5β1 integrin ligand-mediated cell-cell interaction.

15. A method of inhibiting tumor growth, inflammation and/or angiogenesis in a patient, comprising:

administering to said patient an antibody directed against a peptide consisting of SEQ ID No. 41 or consisting of SEQ ID No. 2 that is derived from a cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP) consisting of SEQ ID No. 13, wherein said antibody blocks binding of αvβ3 and/or α5β1 integrins to the cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP), thereby inhibiting tumor growth, inflammation and/or angiogenesis in the patient.

32. A method of inhibiting angiogenesis and the formation of capillaries in a patient in need of such a treatment, comprising:

administering to said patient a pharmacologically effective amount of an antibody directed against a peptide consisting of SEQ ID No. 41 or consisting of SEQ ID No. 2 that is derived from vascular endothelial growth factor and type I collagen inducible protein (VCIP) consisting of SEQ ID No. 13, wherein said antibody inhibits αvβ3 and/or α5β1 integrin-mediated cell-cell interaction, thereby inhibiting angiogenesis and the formation of capillaries in the patient in need of a such a treatment.

*Cited References*

| | | |
|---|---|---|
| Hubbell et al. | US 5,567,440 | Oct. 22, 1996 |
| Cheng et al. | US 5,807,819 | Sep. 15, 1998 |

Vassilev et al., *Inhibition of Cell Adhesion by Antibodies to Arg-Gly-Asp (RGD) in Normal Immunoglobulin for Therapeutic Use (Intravenous Immunoglobulin, IVIg)*, 93 BLOOD 3624-3631 (1999).

Moise Bendayan, *Possibilities of False Immunocytochemical Results Generated by The Use of Monoclonal Antibodies: The Example of the Anti-proinsulin Antibody*, 43 J. HISTOCHEM. CYTOCHEM. 881-886 (1995).

Appellants provide separate argument for claims 8, 15 and 32, so we address the subject matter of each of these independent claims.

*Grounds of Rejection*

1. Claims 8 and 14-15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Vassilev as is evidenced by Bendayan.

2. Claims 15 and 32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cheng, Hubbell and Vassilev as evidenced by Bendayan.

FINDINGS OF FACT

1. The Examiner finds that: "Vassilev *et a1* teach that RGD motif has a central role in mediating cell-to-cell adhesion in a variety of immunological and inflammatory processes (see page 3629, bridging ¶ and page 3624, 2nd col., 1st full ¶ in particular)." (Ans. 3.)

2. The Examiner finds that

> Vassilev *et a1* teach that IVIg contains antibodies to Arg-Gly-Asp (RGD) sequence, and the attachment site of a number of adhesive extracellular matrix proteins, including ligands for β1,

> β3 and β5 integrins (see abstract). Vassilev *et a1* teach a method of inhibiting integrin-dependent platelet aggregation (cell-cell) to fibronectin (Fn) (ligand) "integrin ligand-mediated cell-cell interaction" by anti-RGD antibodies (see page 3626, 1st col., 2nd paragraph and Fig. 4 in particular).

(*Id.*)

3. The Examiner finds that

> Further, adhesion of thrombin-stimulated platelets to von Willebrand factor or Fg (integrin ligand-mediated cell-cell interaction) was completely inhibited by affinity-purified anti-RGD antibodies. Vassilev *et a1* teach that the presence of natural IgG antibodies to the RGD motif may contribute to the immunomodulatory and anti-inflammatory effects of the therapeutic preparations of normal IgG (see abstract). Vassilev *et a1* teach that affinity purified anti-RGD antibodies block the adhesion of Raji cells to Fn. By inhibiting leukocyte adhesion, antibodies in IVIg that recognize the RGD adhesion motif may contribute to the anti-inflammatory effects of IVIg (see page 3629, top ¶).

(*Id.* at 3-4.)

4. Vassilev "teaches that the inhibition of cell adhesion by anti-RGD antibodies can be critical in the Fn matrix formation involving α5/β1 integrins and the subsequent cell adhesion in the progression of metastasis (see page 3629,2nd co., 1st full ¶)." (Ans. 4.)

5. Vassilev "teach that the MoAbs to integrins and adhesion-blocking peptides have been used in experimental models of autoimmune and inflammatory disease as well as the treatment of patients with solid organ allograft rejection (see page 3629, 2nd col. 2nd ¶ in particular)." (*Id.*)

6. Vassilev "teaches that the anti-RGD antibodies bind to peptide and proteins expressing the RGD sequence (see page 3625, 1st col., under Binding assays)." (*Id.*)

7. Vassilev teaches that "the RGD fraction of IVIg bound to fibronectin, fibrinogen, vitronection, VWF and laminin in a dose dependent manner (see Fig. 1 and page 3626, col., 1, top ¶)." (*Id.*)

8. The Examiner finds that, "[g]iven that the claimed SEQ ID NO: 2 and 41 are RGD-containing peptide sequences, the referenced anti-RGD antibodies would bind to the claimed SEQ ID NO: 2 (EGYIQNYRCRGDDSK-VQEAR) and 41 (CRGDD). Moreover, antibodies 'cross-react' with antigens with homolgous [sic] amino acid residues." (*Id.*)

9. Vassilev's "anti-RGD antibody would bind to the peptide comprises SEQ ID NO: 41 (CRGDD) and 2 (EGYIQNYRCRGDDSKVQEAR) due to the shared sequence homology (RGD motif)." (*Id.*)

10. The Examiner finds that

> As is evidenced by Bendayan (J. Histochem. Cytochem. 1995,43:881-886) who characterizes the specific reactivity of a monoclonal antibody produced to human proinsulin, and shows that although the antibody is highly specific, it is nevertheless able to bind to not only human proinsulin, but to proinsulin from other species and even a distinct protein, glucagons, based upon conservation of an Arg-Arg dipeptide sequence in each of these molecules (see entire document).

(Ans. 4.)

11. "Bendayan concludes that 'an antibody directed against such a sequence, although still yielding specific labeling, could reveal different

molecules not related to the original antigen' (page 886, last paragraph in particular)." (*Id.* at 4-5.)

12. The Examiner finds that

> While the prior art teachings may be silent as to the "antibody blocks binding of αvβ3 and/or α5β1 integrins to the cell surface VCIP" per se; the method and the product used in the reference method are the same as the claimed method. Therefore "antibody blocks binding of αvβ3 and/or α5β1 integrins to the cell surface VCIP" is considered inherent properties. The anti-RGD antibodies administered bind to a ligand comprising the RGD motif due to properties inherently possessed by the antibody. That is the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious.

(*Id.* at 5.)

13. "The '819 [Cheng] patent teaches a method of treating angiogenesis comprising administering to the subject RGD-containing peptides (agents) (see abstract and the entire document)." (*Id.* at 6.)

14. "The '819 [Cheng] patent further teaches that angiogenesis is required for the growth of solid tumors and neovascularization serves as a conduit for metastasis (see col. 9, lines 19-21 in particular)." (*Id.*)

15. The Examiner finds that

> Further, the '819 [Cheng] patent teaches methods of using the Arg--Gly--Asp containing peptides such as CRGDDVC (patented SEQ ID NO: 17) to alter αvβ3 integrin receptor-mediated binding of a cell . . . to a matrix. The '819 [Cheng] patent teaches further teaches methods for ameliorating the severity of a pathology characterized by an undesirable level of angiogenesis in a subject using RGD-containing peptides (see the entire document including the abstract).

(Ans. 6.)

16. "The claimed invention differs from the '819 [Cheng] patent teachings only by the recitation of antibody to SEQ ID NO: 2 or 41 in claims 15 and 32." (*Id.*)

17. "The '440 [Hubbell] patent teaches that cell adhesion plays an important role in human disease. These interactions proceed by the interaction of receptors upon the surface of a cell with proteins or glycosaminoglycans upon the surface of another cell or within the extracellular matrix." (*Id.*)

18. "The '440 [Hubbell] patent further teaches that routes to the interruption of these interactions typically involve competitive inhibition of these receptor-ligand interactions, for example, with antibodies, soluble ligands which act as receptor antagonists (e.g., cyclic RGD peptides), soluble receptors, or other competitors (see col. 1, lines 17-30 in particular)." (*Id.*)

19. "Vassilev *et a1* teach a method of inhibiting integrin-dependent platelet aggregation 'cell-cell interaction' to Fn (integrin ligand-mediated cell-cell interaction) by anti-RGD antibodies (see page 3626, 1st col., 2nd paragraph and Fig. 4 in particular)." (*Id.*)

20. The Examiner finds that "Vassilev *et a1* further teach that . . . cyclic RGD peptides have been shown to inhibit α4β1-dependent adhesion of T cells to cytokine-activated endothelial cells (see page 3629, 1st col., last paragraph to the 2nd col., 1st paragraph in particular)." (Ans. 6-7.)

21. "The limitation 'blocks the binding of αvβ3 and/or α5βl integrins to cell surface VCIP' would be expected properties of the resultant method." (*Id.* at 7.)

22. The Examiner finds that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the

CRGDDVC cyclic peptide taught by the '819 [Cheng] patent with anti-RGD antibody taught by Vassilev *et al* in a method of inhibiting angiogenesis in a subject." (*Id.*)

23. The Examiner finds that

> One of ordinary skill in the art at the time the invention was made would have been motivated to do so because routes to the interruption of cell-cell interactions typically involve competitive inhibition of these receptor-ligand interactions with either receptor antagonists (e.g., cyclic RGD peptides), antibodies or other competitors as taught by the '440 [Hubbell] patent.

(Ans. 7.)

24. The Examiner finds from the combined teachings of the references, "that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention." (*Id.*)

*Claim Interpretation*

During ex parte prosecution, claims are to be given their broadest reasonable interpretation consistent with the description of the invention in the specification. *See In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989).

"Without evidence in the patent specification of an express intent to impart a novel meaning to a claim term, the term takes on its ordinary meaning." *Optical Disc Corp. v. Del Mar Avionics*, 208 F.3d 1324, 1334 (Fed. Cir. 2000). In addition, "[t]he ordinary and customary meaning of a claim term may be determined by reviewing a variety of sources. Some of these sources include the claims themselves; dictionaries and treatises; and the written description, the drawings, and the prosecution history."

*Brookhill-Wilk, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298 (Fed. Cir. 2003).

The steps of the method of claim 8 include:
contacting cells with an antibody "directed against" a peptide consisting of SEQ ID NO: 41 or consisting of SEQ ID No. 2.

The term "directed against," in the context of antibody/antigen binding, means that an antibody binds to a particular antigen. Thus, we conclude that an antibody within the scope of the claim must have cross-reactivity with a peptide consisting of SEQ ID NO: 41 or consisting of SEQ ID No. 2, since Appellants have provided no special definition of the term "directed against" in the Specification.

*Anticipation*

1. Claims 8 and 14-15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Vassilev as is evidenced by Bendayan.

ISSUE

The Examiner finds that Vassilev discloses each element claimed.

Appellants contend that Vassilev does not teach a method of inhibiting tumor growth, inflammation, and/or angiogenesis in a patient. Appellants argue that Vassilev does not teach blocking the interaction between αvβ3 and/or α5β1 integrins to the cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP), thereby inhibiting the αvβ3 and/or α5β1 integrin ligand-mediated cell-cell interaction.

The issue is: Have Appellants demonstrated error in the Examiner's anticipation rejection?

PRINCIPLES OF LAW

In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. *See In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997).

Moreover:

> *Where . . . the claimed and prior art products are identical or substantially identical,* or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product…. Whether the rejection is based on "inherency" under 35 U.S.C. § 102, on "prima facie obviousness" under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products.

*In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) (emphasis added).

"From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing." *In re Papesch*, 315 F.2d 381, 391 (CCPA 1963).

*Principles of Law for remaining obviousness rejections*

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a *prima facie* case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or

argument shift to the applicant." *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citations omitted). In order to determine whether a prima facie case of obviousness has been established, we consider the factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966): (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the relevant art; and (4) objective evidence of nonobviousness, if present.

"[O]bviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)).

"[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991).

## ANALYSIS

Appellants contend that Vassilev does not teach a method of inhibiting tumor growth, inflammation, and/or angiogenesis in a patient. (App. Br. 12.) Appellants argue that Vassilev does not teach blocking the interaction between αvβ3 and/or α5β1 integrins to the cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP), thereby inhibiting the αvβ3 and/or α5β1 integrin ligand-mediated cell-cell interaction. Appellants also argue that Vassilev does not teach the specific peptide sequences of SEQ ID NOs: 2 and 41. (App. Br. 12.)

We essentially agree with the Examiner's fact finding, statement of the rejection and responses to Appellants' arguments as set forth in the Answer. We adopt them as our own. In particular, with respect to

Appellants' arguments for integrin binding of claim 8 and for tumor growth and inflammation for claim 15, the Examiner responds that:

> Vassilev et al teach the ability of the anti-RGD antibodies in IVIg to inhibit integrin-dependent platelet aggregation to fibronectin (Fn) (integrin ligand-mediated cell-cell interaction) (see Fig. 4, page 3627). . . . Specifically, Vassilev *et a1* teach IVIg contains antibodies to the Arg-Gly-Asp (RGD) sequence, and the attachment site of a number of adhesive extracellular matrix proteins, including ligands for β1, β3 and β5 integrins. Anti-RGD $F(ab')_2$ antibodies inhibited the adhesion of activated α4β1 integrin-expressing B cells to Fn. . . . Regarding tumor growth, claim 15 recites the conditions "tumor growth, inflammation and/or angiogenesis" in the alternative. In this case, there is no requirement for the prior art to meet all the claimed conditions. Yet, Vassilev teach that integrins play a critical role in inflammation, immune responses, thrombosis, malignant transformation, and metastasis (see page 3624, 2nd col., 1st ¶). ["]Metastasis formation was shown to be suppressed by agents interfering with RGD-dependent adhesion in several animal models and in vitro models by using human tumoral cells. MoAbs to integrins and adhesion-blocking peptides have been used in experimental models of autoimmune and inflammatory diseases as well as in the treatment of patients with solid organ allograft rejection. Because human IgG autoantibodies recognizing the same target molecules as these MoAbs are present in IVIg, we speculate that IVIg may have similar in vivo effects["] (see p. 3629, 1st full ¶).

(Ans. 8-9.)

Thus, Vassilev teaches an antibody to a sequence, RGD. The method of Claim 8 requires contacting cells with an antibody with cross-reactivity to SEQ ID NO: 41 ("CRGDD"). We conclude that the Examiner has provided sufficient evidence that the Vassilev antibody to the RGD sequence would have the same or substantially the same cross-reactivity and integrin binding

as the claimed antibody to "CRGDD" to shift the burden of proof under *In re Best*, to provide evidence that the two antibodies do not possess the same properties or ability to inhibit αvβ3 and/or a5β1 integrin ligand-mediated cell-cell interaction. Appellants have not provided evidence that the Vassilev antibodies and the claimed antibodies do not possess the same properties or ability to inhibit αvβ3 and/or a5β1 integrin ligand-mediated cell-cell interaction of claim 8, or anti-tumor or anti-inflammatory properties of claim 15.

Appellants argue that Vassilev teaches inhibiting platelet aggregation (App. Br. 11) and that "inhibiting platelet aggregation by a pool of naturally occurring antibodies is not the equivalent of inhibiting αvβ3 and/or α5β1 integrin ligand-mediated cell-cell interaction nor the same as inhibiting tumor growth, inflammation and/or angiogenesis in a patient, as recited in Appellants' claims 8 and 15." (App. Br. 11.)

The Examiner does not find this argument persuasive because

> Vassilev *et al* teach that these antibodies are relevant for the immunomodulatory effects of IVIg in autoimmune and inflammatory diseases and for understanding the role of normal IgG in immune homestasis (see page 3624, 2nd col., 2nd full ¶) Vassilev *et a1* teach that the RGD motif has a central role in mediating cell-to-cell and cell-matrix adhesion in a variety of immunological and inflammatory processes (see page 3629, bridging ¶). With respect to the antibody, Vassilev *et a1* teach that the anti-RGD antibodies bind to AVTGRGDSPA peptide and to proteins expressing the RGD sequence, such as the RGD containing Fn, vitronectin, fg, and vWF (see pp. 3625, 1st col., under *Binding assays*). Given that the claimed SEQ ID NO: 2 and 41 are RGD-containing peptides, wherein the RGD motif has a central role in mediating cell-to-cell adhesion, the referenced anti-RGD antibodies would bind to the claimed

> SEQ ID NO: 2 (EGYIQNYRCRGDDSKVQEAR) and 41 (CRGDD) irrespective of how the antibodies were obtained.

(Ans. 9-10.) We agree one of ordinary skill in the art reviewing the disclosure of Vassilev would understand that the Vassilev antibodies possess immunomodulatory effects relevant to inflammatory diseases, as in claim 15.

In addition, Appellants argue that "Vassilev *et al.* do not teach blocking the interaction between VCIP and the αvβ3 and α5β1 integrins. Also, Vassilev *et al.* do not teach VCIP or αvβ3 and/or α5β1 integrins." (App. Br. 11.)

We do not find this argument persuasive. The Examiner provides evidence that:

> Although the reference is silent about blocking the binding of αvβ3 and/or α5β1 integrins to VCIP, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. … On this record, it is reasonable to conclude that the same patient is being administered the same active anti-RGD antibodies by the same mode of administration in the same amount in both the instant claims and the prior art reference. The fact that applicant may have discovered yet another beneficial effect from the method set forth in the prior art does not mean that they are entitled to receive a patent on that method. The claimed functional limitations would be inherent properties of the referenced methods to administer anti-RGD antibodies to treat inflammation. Vassilev *et a1* teach that the RGD motif has a central role in mediating cell-to-cell adhesion in a variety of immunological and inflammatory process (see page 3629, bridging ¶) The claimed method recites inhibition of "αvβ3 and/or α5β1 integrin ligand-mediated cell-cell interaction". Vassilev *et al* teachings the inhibition of platelets aggregation (cell-cell) to fibronectin (ligand) is integrin ligand-

> mediated cell-cell interaction as recited in the preamble of the claim. The integrin being αvβ3 and/or α5βl is inherent to the platelets. Platelets do express both αvβ3 and α5β1 in addition to the αIIbβ3. [Vassilev, 3626 and 3629.] That is the anti-RGD antibodies bind to an RGD-containing ligand mediated platelet aggregation (cell-cell interaction) which would lead to the inhibition of the aggregation. The integrin being αvβ3, α5βl or αIIbβ3 is inherent. Both the claimed and the prior art invention are directed to a single method step of inhibiting integrin ligand-mediated cell-cell interaction with anti-RGD antibodies. The prior art anti-RGD antibodies would bind to claimed SEQ ID NOS: 2 and 41, the cell surface integrins including αvβ3 and α5β1 that recognize the RGD motif would inherently be inhibited in the method. The ligand being VCIP, which is an RGD-containing protein, is inherent in the method which contributes to inflammation. The teaching of record has properly shifted burden to applicant.

(Ans. 10-11.)

Appellants argue that their anti-VCIP-RGD antibody does not react with mouse antigens, referencing the Specification, page 40. (App. Br. 13.) The Specification does not specifically indicate which mouse antigens their antibody did not react with. Again, Appellants have not provided appropriate comparative evidence with the closest prior art, that is, evidence showing that the Vassilev antibodies do not possess the properties recited in the claims. No Reply Brief was filed by Appellants in response to the Examiner's arguments.

## CONCLUSION OF LAW

Appellants have not demonstrated error in the Examiner's anticipation rejection.

*Obviousness*

2. Claims 15 and 32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cheng, Hubbell and Vassilev as evidenced by Bendayan.

## ISSUE

The Examiner finds that it would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the CRGDDVC cyclic peptide taught by Cheng with the anti-RGD antibody taught by Vassilev *et al* in a method of inhibiting angiogenesis in a subject.

Appellants contend that one of ordinary skill in the art would not have had a reasonable expectation of success of inhibiting tumor growth, inflammation and/or angiogenesis upon review of the cited references. (App. Br. 15.) Appellants argue that one of ordinary skill in the art would not have been able to predict that VCIP would function as an integrin ligand.

The issue is: Have Appellants demonstrated error in the Examiner's obviousness rejection?

## ANALYSIS

Appellants contend that one of ordinary skill in the art would not have had a reasonable expectation of success of inhibiting angiogenesis upon review of the cited references. (App. Br. 15.)

We essentially agree with the Examiner's fact finding, statement of the rejection and responses to Appellants' arguments as set forth in the Answer.

With respect to claim 32, the Examiner finds that the combined prior art and Appellants administer the same antibody to the same patient to

achieve the same results. (Ans. 14-15.) We agree with the Examiner that one of ordinary skill in the art reviewing the cited references would have understood that anti-RGD antibodies could be administered to a patient to inhibit angiogenesis. (See particularly, Cheng, col. 12, ll. 56-61.) We conclude that the Examiner has provided sufficient evidence that the antibodies to the RGD sequence of the combination of the cited references would have the same or substantially the same cross-reactivity and anti-angiogenesis properties as the claimed antibody to "CRGDD" to shift the burden of proof under *In re Best*, to provide evidence that the two antibodies do not possess the same anti-angiogenesis properties. Appellants have not provided such evidence. All that is required by the patent law is a reasonable expectation of success, not absolute predictability of success. *See In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). A reasonable expectation is provided by the combination of the cited references indication that the anti-RGD antibodies are useful in the treatment of angiogenesis.

## CONCLUSION OF LAW

Appellants have not demonstrated error in the Examiner's obviousness rejection.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

## AFFIRMED

cdc

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